

Immune Reconstitution Inflammatory Syndrome Unmasking Cerebral Toxoplasmosis after Restarting Dolutegravir-Based Antiretroviral Therapy: A Case Report and Mini-Review

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Abstract

A 42-year-old woman living with HIV, who had been off antiretroviral therapy for two years, restarted a dolutegravir-based regimen with a baseline plasma viral load of 120,000 copies/mL and a CD4 T-lymphocyte count of 64 cells/mm³. Two months later, despite complete virological suppression and a CD4 count of 201 cells/mm³, she developed headache, seizures, and a motor deficit. Cranial computed tomography (CT) revealed ring-enhancing lesions suggestive of cerebral toxoplasmosis. The timing of events and the rapid virological response led to a diagnosis of immune reconstitution inflammatory syndrome (IRIS) unmasking cerebral toxoplasmosis. The outcome was favourable with co-trimoxazole, corticosteroid therapy, and continuation of antiretroviral therapy. This case highlights the importance of considering IRIS in patients presenting with neurological manifestations after initiation or resumption of effective antiretroviral therapy.

Keywords

IRIS, Toxoplasmosis, Dolutegravir

1. Introduction

Toxoplasmosis is caused by the obligate intracellular parasite *Toxoplasma gondii*.

It remains the most common opportunistic infection of the central nervous system in people living with HIV [1]. The absence of primary co-trimoxazole prophylaxis in HIV-positive patients is the main factor predisposing to its occurrence [2] [3]. With the introduction of integrase inhibitor-based regimens, such as dolutegravir, as first-line antiretroviral therapy in WHO guidelines [4], the incidence of immune reconstitution inflammatory syndrome has increased [5] [6]. This is further compounded in sub-Saharan Africa by the late entry of HIV-positive patients into care, often at an advanced stage of disease [7] [8].

2. Case Report

A 42-year-old woman with HIV infection was followed on an outpatient basis at a dedicated HIV care facility. She began antiretroviral therapy in June 2013 with a regimen of tenofovir, emtricitabine, and efavirenz (Atripla®). This regimen was replaced on 28 January 2020 with an ART combination of tenofovir, lamivudine, and dolutegravir following documented treatment failure. She had a history of poor adherence, with repeated treatment interruptions; her last clinic visit before the current episode was on 12 May 2023. She resumed antiretroviral therapy (Acriptega®) and co-trimoxazole chemoprophylaxis on 22 January 2026, after therapeutic education sessions deemed successful and after a clinical and laboratory work-up that was unremarkable except for a plasma viral load of 120 000 copies/mL and a CD4 T-lymphocyte count of 64 cells/mm³, both recorded on 22 January 2026. The therapeutic education involved assessing adherence to antiretroviral therapy using the Morisky Medication Adherence Scale-8 (MMAS-8). These sessions were conducted with the psychologist and scheduled as follows: two weeks before the resumption of antiretroviral therapy (one session), at the time of resumption (one session), and subsequently once a month (two sessions). A total of four sessions were held; the MMAS-8 score was <6 (indicating poor adherence) at the first session, and 8, 8, and 8 (indicating good adherence) at the subsequent sessions, respectively.

On 18 February 2026, she was admitted to another health facility with headache and fever. The rest of the clinical examination was unremarkable. Plasma viral load at that time was 420 copies/mL. A lumbar puncture was performed. Thick blood smear microscopy for hemoparasites was positive, with a parasite density of 10.000 parasites/μL. India ink staining of the cerebrospinal fluid for *Cryptococcus* was negative, as were other bacteriological investigations. She was treated for malaria with artesunate, remained hospitalized for two days, and was discharged on an artemisinin-based combination therapy instead of artesunate. She continued her usual antiretroviral therapy and co-trimoxazole chemoprophylaxis.

On 28 March 2026, following a fall and seizures, the patient was admitted to our department. On admission, clinical examination showed:

- A conscious patient, fully oriented to time and place, with a Glasgow Coma Scale score of 15/15;

- Anorexia and asthenia;
- Blood pressure 110/80 mmHg, heart rate 97 beats per minute, oxygen saturation 96% on room air;
- Fever at 37.9°C;
- Oral candidiasis;
- Headache;
- Tonic-clonic seizures;
- Left hemibody motor deficit, with muscle strength graded 3/5 in the left upper and lower limbs.

Further work-up revealed the following:

- Cranial CT: multiple bilateral infratemporal hypodense lesions surrounded by a contrast-enhancing hyperdense rim, consistent with a “ring” (cocarde) pattern, with perilesional oedema (**Figure 1**);
- GeneXpert MTB/RIF® on gastric aspirate: negative;
- Tuberculin skin test: 1 mm induration (read more than 72 hours after subcutaneous injection);
- Thick blood smear for haemoparasites: negative;
- Creatinine 9.5 mg/L, urea 0.22 g/L, ALT 10 IU/L (normal), AST 24.7 IU/L (normal);
- Plasma viral load on 1 April 2026: undetectable;
- CD4 T-lymphocyte count: 201 cells/mm³;
- Chest radiograph: within normal limits;
- Complete blood count: haemoglobin 10 g/dL, white blood cells $6.03 \times 10^3/\mu\text{L}$, platelets $298 \times 10^3/\mu\text{L}$.

Based on these findings and the clinical timeline, a diagnosis of immune reconstitution inflammatory syndrome (IRIS) unmasking cerebral toxoplasmosis was considered. After intravenous access was obtained, initial management consisted of:

- Co-trimoxazole (sulfamethoxazole/trimethoprim) 960 mg tablets, two tablets three times daily;
- Dexamethasone 20 mg/day;
- Phenobarbital 200 mg/day;
- Diazepam 10 mg as needed for seizures;
- Fluconazole 100 mg/day;
- Continuation of antiretroviral therapy: Acriptega® (TDF/3TC/DTG), one tablet daily.

The clinical course was marked by cessation of seizures and improvement of the motor deficit to 5/5 in the left hemibody. The patient was discharged after two weeks of hospitalisation, with continued clinical follow-up. At the follow-up visit one month after discharge, the patient reported good adherence to antiretroviral therapy and cotrimoxazole, confirmed by an MMAS-8 score of 8. Rehabilitation had also been initiated to continue functional recovery. No signs of recurrence were reported at this visit.

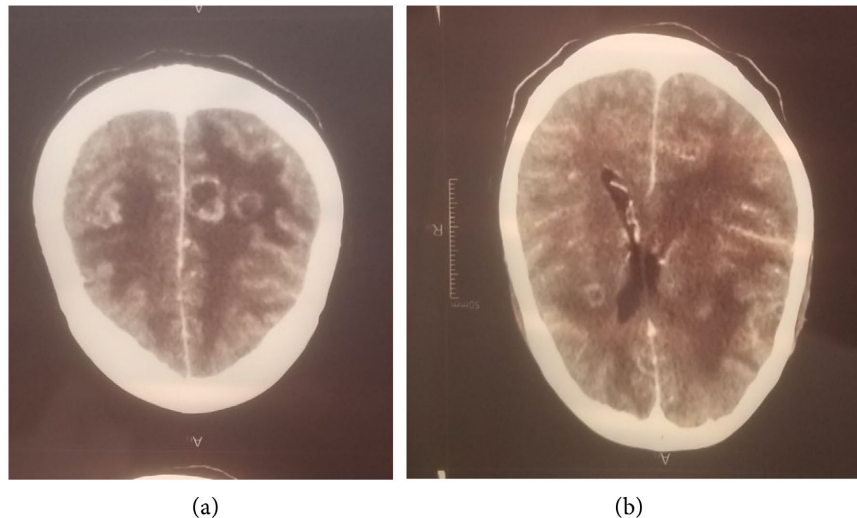


Figure 1. Ring-enhancing lesions with perilesional oedema (a and b) demonstrated on cranial CT in our patient.

3. Discussion

Cerebral toxoplasmosis and unmasking IRIS were presumptive diagnoses based on the clinical, radiological, immunological, virological, and therapeutic-response evidence, in the absence of microbiological or histological confirmation. Indeed, the onset of a neurological syndrome in the context of rapid immune reconstitution during antiretroviral therapy fits the diagnostic criteria proposed for immune reconstitution inflammatory syndrome (IRIS) [9]—characterized by a rapid rise in CD4 lymphocyte counts and a drop in viral load, as well as specific clinical and neuroimaging features. The favorable clinical course under cotrimoxazole—marked by the cessation of seizures and the resolution of neurological deficits within two weeks—provides strong diagnostic evidence for cerebral toxoplasmosis. This therapeutic response makes other etiologies for ring-enhancing brain lesions, such as primary CNS lymphoma, tuberculoma, and neoplastic lesions, less likely.

Immune reconstitution inflammatory syndrome (IRIS) occurs within the first months after initiation of antiretroviral therapy or after a change in regimen, affecting approximately 10% - 32% of HIV-positive patients [10]-[12]. At initiation of antiretroviral therapy, neurological manifestations are common, with about a quarter attributable to IRIS and a predominance of tuberculosis and cryptococcosis [13]. Reports of toxoplasmosis-associated IRIS are increasing in the global literature, although they remain rare in Africa.

IRIS should be suspected when a patient's clinical status deteriorates after initiation of antiretroviral therapy, either in a paradoxical form—when the underlying condition was already known and treated before starting antiretroviral therapy—or in an unmasking form [12]. Clinical presentation depends on the underlying condition(s). The clinical features of cerebral toxoplasmosis occurring as IRIS are similar to those of ordinary cerebral toxoplasmosis, with subacute onset

of headache, focal neurological deficits (the pattern depending on the site of central nervous system involvement), and variable alteration of consciousness, together with a suggestive pattern on cranial CT, occurring in a context of profound immunosuppression [14]. For IRIS, a rapid decline in viral load together with a rise in CD4 count supports the diagnosis.

We report the case of a patient who had been off treatment for two years and who, two months after resuming antiretroviral therapy, developed immune reconstitution inflammatory syndrome unmasking cerebral toxoplasmosis. In our resource-limited setting, this diagnosis was supported by evidence of severe immunosuppression, marked virologically by an HIV viral load of 120,000 copies/mL and a CD4 count of 64 cells/mm³ before resumption of antiretroviral therapy; by the kinetics of the plasma HIV viral load, which became undetectable after one month of treatment; by the rise in CD4 count to 201 cells/mm³; and by the appearance of neurological and radiological features suggestive of cerebral toxoplasmosis. A diagnosis of cerebral toxoplasmosis with an undetectable viral load is unusual. The imaging findings were typical of ordinary cerebral toxoplasmosis, showing an abscess-like image with perilesional oedema.

Current WHO guidelines recommend dolutegravir-based regimens as first-line treatment for people living with HIV. Integrase inhibitors, such as dolutegravir, produce a rapid decline in viral load and reconstitution of the CD4 T-lymphocyte pool [15] [16]; these biological changes are associated with an increased risk of IRIS, particularly in patients presenting at an advanced stage of disease with severe immunosuppression [17]-[19]. Among studies reporting cases of IRIS, few have described toxoplasmosis-associated IRIS, whether before [3] [7] [8] [17] [20]-[22] or after [6] [18]-[20] integrase inhibitor-containing regimens became the preferred protocols. Most of these studies were conducted in high-income countries.

Several factors converge in the African context: 1) adoption by most countries of WHO recommendations favouring dolutegravir-based combinations as preferred treatment [23]; 2) a persistently high number of patients presenting at an advanced stage of AIDS [20] [22] [24]; 3) toxoplasmosis is among the most common conditions in patients presenting at an advanced stage [20] [21] [25]-[28]; and 4) patients started on dolutegravir-based regimens in Africa also experience rapid decline in plasma viral load and rapid CD4 reconstitution [19]. Despite these factors, data on unmasking or paradoxical IRIS related to toxoplasmosis remain scarce or absent. WHO guidelines identify cryptococcosis and tuberculosis as conditions for which initiation of antiretroviral therapy should be deferred until the opportunistic infection is treated; patients with toxoplasmosis, in contrast, may start antiretroviral and antitoxoplasmic therapy concomitantly. Difficulties related to the work-up required for diagnosis—particularly limited access, in some settings, to radiological investigations and to baseline viral load testing (which is not routinely recommended at antiretroviral therapy initiation)—contribute to the scarcity of data supporting the diagnosis of toxoplasmosis-associated IRIS.

4. Conclusion

Cerebral toxoplasmosis associated with immune reconstitution inflammatory syndrome remains a rare but potentially severe complication in people living with HIV. This case underscores the need to suspect IRIS in patients presenting with neurological manifestations after initiation or resumption of effective antiretroviral therapy, particularly in those with advanced immunosuppression. Better documentation of such cases in sub-Saharan Africa is needed to improve the understanding, diagnosis, and management of this still under-reported entity.

Author Contributions

Martin Herbas Ekat: Conceptualization, clinical management, and writing the original draft. **Tatia Adoua Doukaga:** Clinical management and validation of the final version. **Gilus Axel Aloumba:** Critical revision of the manuscript. **Amona Médard:** Radiological interpretation and Critical revision of the manuscript. **Bienvenu Rolland Ossibi Ibara:** Radiological interpretation and supervision.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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